

CLAIMS LISTING

1. (Cancelled) An ~~es~~ ~~dentritic~~ ~~cell~~.
2. (Cancelled) ~~The cell of claim 1 which is genetically modified.~~
3. (Cancelled) ~~The cell of claim 1 or claim 2 which is immature.~~
4. (Cancelled) ~~The cell of claim 1 or claim 2 which is mature.~~
5. (Cancelled) ~~A genetically modified immature dentritic cell which is capable of maturation.~~
6. (Cancelled) ~~The cell of any one of the preceding claims which is human.~~
7. (Cancelled) ~~The cell of any one of the preceding claims which is lymphoid.~~
8. (Cancelled) ~~The cell of any one of claims 1 to 6 which is myeloid.~~
9. (Cancelled) ~~The cell of any one of the preceding claims which is primary.~~
10. (Cancelled) ~~The cell of any one of the preceding claims which is isolated or substantially pure.~~
11. (Cancelled) ~~The cell of any one of the preceding claims which expresses one or more heterologous gene(s).~~
12. (Cancelled) ~~The cell of claim 11 wherein the heterologous gene(s) encode a protein which has an immunomodulatory effect.~~
13. (Cancelled) ~~The cell of claim 11 wherein the protein is a cell surface receptor.~~
14. (Cancelled) ~~The cell of claim 11 wherein the protein is Fas ligand.~~
15. (Cancelled) ~~The cell of claim 11 wherein the gene expresses a dominant negative form of an endogenous protein.~~
16. (Cancelled) ~~The cell of claim 11 wherein the protein is an antigen target for the immune system, such as an autoantigen, a tumour antigen, or a foreign antigen for example a microbial or viral antigen.~~
17. (Cancelled) ~~The cell of any one of claims 11 to 16 wherein the cell co-expresses two or more heterologous genes.~~
18. (Cancelled) ~~The cell of claim 17 wherein one of the heterologous genes prolongs the life span of the cell.~~
19. (Cancelled) ~~The cell of claim 18 wherein the gene is an anti-apoptotic gene.~~
20. (Cancelled) ~~The cell of claim 18 or 19 wherein the gene encodes FLIP or bcl-2.~~

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21. (Cancelled) ~~The cell of any one of the preceding claims in which one or more endogenous gene(s) have been inactivated.~~
22. (Cancelled) ~~The cell of claim 21 wherein the inactivated endogenous gene(s) comprise any of: B7-1, IL-12, the p35 or p40 subunit of IL-12.~~
23. (Cancelled) ~~A composition comprising the cell of any one of the preceding claims.~~
24. (Cancelled) ~~The composition of claim 23 which is a pharmaceutical composition.~~
25. (Cancelled) ~~The composition of claim 23 or 24 further comprising a pharmaceutical excipient.~~
26. (Cancelled) ~~The cell of any one of the preceding claims, for use in therapy or prophylaxis.~~
27. (Cancelled) ~~Use of the cell of any one of the preceding claims for the manufacture of a medicament for use in therapy or prophylaxis.~~
28. (Cancelled) ~~A process for the manufacture of a medicament for use in therapy characterized in the use, as an essential constituent of said composition, of the cell of any one of claims 1 to 22.~~
29. (Cancelled) ~~The cell of any one of claims 1 to 26, use of claim 27 or process of claim 28 wherein the therapy or prophylaxis is immunotherapy.~~
30. (Cancelled) ~~The invention of claim 29 wherein the immunotherapy comprises immunostimulation.~~
31. (Cancelled) ~~The invention of claim 29 or claim 30 wherein the immunostimulation comprises tumour immunotherapy or vaccination against infectious agents.~~
32. (Cancelled) ~~The invention of claim 29 wherein the immunotherapy comprises down-modulation of a detrimental immune response.~~
33. (Cancelled) ~~The invention of claim 32 wherein the down-modulation of a detrimental immune response is in the treatment of autoimmune disease or allograft rejection.~~
34. (Cancelled) ~~The invention of claim 29 wherein the immunotherapy comprises altering dendritic cell function.~~

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35. (Cancelled) ~~The invention of claim 19 or 34 wherein the immunotherapy comprises inducing a Th1 to Th2 immune deviation (for example in the treatment of autoimmune diseases and disorders).~~
36. (Cancelled) ~~A method for producing dendritic cells which method comprises:~~
 - ~~i) providing a population of embryonic stem cells; ii) culturing the embryonic stem cells in the presence of a cytokine or combination of cytokines which bring about differentiation of the embryonic stem cells into dendritic cells; and iii) recovering the dendritic cells from the culture.~~
37. (Cancelled) ~~The method according to claim 36, wherein the cytokine or combination of cytokines is or includes IL-3.~~
38. (Cancelled) ~~The method according to claim 37, wherein a combination of cytokines including IL-3 and GM-CSF is used.~~
39. (Cancelled) ~~The method according to any one of claims 36 to 38, wherein the embryonic stem cells in i) are in the form of embryoid bodies.~~
40. (Cancelled) ~~The method according to any one of claims 36 to 38, wherein the embryonic stem cells are genetically modified.~~
41. (Cancelled) ~~The method according to claim 40, wherein the embryonic stem cells are transfected with at least one gene which is expressed in the dendritic cells.~~
42. (Cancelled) ~~The method according to claim 41, wherein the gene is under the control of a promoter which initiates or upregulates gene expression on maturation of dendritic cells, such as the CD11c promoter.~~
43. (Cancelled) ~~The method according to claim 41 or 42, wherein the gene is a reporter gene which expresses a detectable product in the dendritic cells.~~
44. (Cancelled) ~~The method according to claim 43, wherein the gene encodes a fluorescent product.~~
45. (Cancelled) ~~The method according to claim 44, wherein the gene is the GFP gene.~~
46. (Cancelled) ~~The method according to claim 41 or 42, wherein the gene expresses a protein which has an immunomodulatory effect.~~
47. (Cancelled) ~~The method according to claim 46, wherein the protein is a cell surface receptor.~~
48. (Cancelled) ~~The method according to claim 47, wherein the protein is Fas ligand.~~

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49. (Cancelled) ~~The method according to claim 46, wherein the gene expresses a dominant negative form of an endogenous protein.~~
50. (Cancelled) ~~The method according to claim 46, wherein the protein is an antigen target for the immune system, such as an autoantigen, a tumour antigen, or a foreign antigen for example a microbial antigen.~~
51. (Cancelled) ~~The method according to claim 40, wherein the ES cells are genetically modified so as to inactivate at least one copy of at least one gene, for example by homologous recombination or antisense technology.~~
52. (Cancelled) ~~The method according to claim 51, wherein the inactivated gene is a gene normally involved in dendritic cell function, such as a gene encoding the p35 or p40 subunit of IL-12.~~
53. (Cancelled) ~~The method according to any one of claims 36 to 52, wherein the ES cells contain a gene which functions to prolong the lifespan of dendritic cells, such as the gene encoding bcl-2 or FLIP.~~
54. (Cancelled) ~~The method according to any one of claims 36 to 53, wherein the recovered dendritic cells are substantially pure.~~
55. (Cancelled) ~~The method according to any one of claims 36 to 54, wherein the ES cells are derived from a mouse strain such as CBA/Ca or C57131/6.~~
56. (Cancelled) ~~The method according to claim 55, wherein the ES cells are from the ESF1 16 cell line.~~
57. (Cancelled) ~~Dendritic cells produced by (or obtainable by) the method according to any one of claims 36 to 56.~~
58. (Cancelled) ~~A population of embryonic stem cells for use in the method according to any one of claims 36 to 56.~~
59. (Cancelled) ~~A population of genetically modified embryonic stem cells in which a gene normally expressed in dendritic cells has been inactivated.~~
60. (Cancelled) ~~A population of genetically modified embryonic stem cells transfected with a nucleic acid comprising a promoter operably linked to a coding sequence, wherein the promoter initiates or upregulates expression of the coding sequence on maturation of dendritic cells.~~

61. ~~(Cancelled) A method for investigating a mammalian gene, which method comprises generating a test population of dendritic cells from a population of embryonic stem cells and comparing the test dendritic cells to a population of control dendritic cells which differ from the test dendritic cells in respect of the gene.~~
62. ~~(Cancelled) A process for producing a pharmaceutical composition (e.g. an immunotherapeutic composition) comprising the steps of: (a) providing a test system comprising the cell of any one of claims 1 to 22 (or a component thereof); (b) providing candidate drugs; (c) screening the candidate drugs by contacting the test system with one of the candidate drugs and analysing the interaction of the candidate drug with the test system, wherein the nature of the interaction is an index of pharmaceutical activity, and optionally (d) synthesising or purifying a drug having pharmaceutical activity on the basis of the identity of the candidate drug screened in step (c).~~
63. ~~(Cancelled) A process for screening candidate drugs for pharmaceutical activity (e.g. immunotherapeutic activity) comprising the steps of: (a) providing a test system comprising the cell of any one of claims 1 to 22 (or a component thereof); (b) providing candidate drugs; (c) screening the candidate drugs by contacting the test system with one of the candidate drugs and analysing the interaction of the candidate drug with the test system, wherein the nature of the interaction is an index of pharmaceutical activity.~~
64. (Currently Amended) A process for producing a long-term culture of immature dendritic cells, which process comprises:
- (i) ~~providing a population of embryonic stem cells;~~(ii)
culturing the embryonic stem cells in the presence of a
~~cytokine or combination of cytokines~~ of a composition comprising
IL-3, which bring about differentiation of the embryonic stem cells
into immature dendritic cells whose protracted longevity and capacity
for self renewal produce a long-term culture of immature dendritic
cells; and (iii) recovering immature dendritic cells from the culture,
which immature dendritic cells are capable of maturation to an
immunostimulatory phenotype.

65. (Cancelled) ~~The process of claim 64 further comprising the step (iv) of inducing the immature dendritic cells to mature thereby producing mature immunostimulatory dendritic cells.~~
66. (Cancelled) ~~The process of claim 65 wherein the immature dendritic cells are stimulated to mature with an inflammatory mediator.~~
67. (Cancelled) ~~The process of claim 65 wherein the inflammatory mediator is LPS.~~
68. (Previously presented) The process according to claims 64, wherein the cytokine or combination of cytokines is or includes IL-3.
69. (Previously presented) The process according to claim 68, wherein a combination of cytokines including IL-3 and GM-CSF is used.
70. (Previously presented) The process according to claim 64, wherein the embryonic stem cells in (i) are in the form of embryoid bodies, generated by culturing purified embryonic stem cells in suspension for 14 days in the absence of recombinant leukemia inhibitory factor.
71. (Previously presented) The process according to claim 64, wherein the embryonic stem cells are genetically modified.
72. (Previously presented) The process of claim 71, wherein the cells express one or more heterologous gene(s).
73. (Previously presented) The process of claim 72, wherein the heterologous gene (s) encode a protein which has an immunomodulatory effect.

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74. (Previously presented) The process of claim 73, wherein the protein is a cell surface receptor.
75. (Previously presented) The process of claim 74, wherein the protein is Fas-ligand.
76. (Previously presented) The process of claim 72, wherein the gene(s) express a dominant negative form of an endogenous protein.
77. (Previously presented) The process of claim 73, wherein the protein is an antigen target for the immune system, such as an autoantigen, a tumour antigen, or a foreign antigen.
78. (Previously presented) The process of claim 64, wherein the cell co-expresses two or more heterologous genes.
79. (Previously presented) The process of claim 78, wherein one of the heterologous genes prolongs the life-span of the cell.
80. (Previously presented) The process of claim 79, wherein the gene is an anti-apoptotic gene.
81. (Previously presented) The process of claim 78 or 79, wherein the gene encodes FLIP or bcl-2.
82. (Previously presented) The process of claim 64, in which one or more endogenous gene (s) have been inactivated.
83. (Previously presented) The process of claim 82, wherein the inactivated endogenous gene (s) comprise any of: B7-1, IL-12, the p35 or p40 subunit of IL-12.

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84. (Previously presented) The process of claim 71, wherein the embryonic stem cells are transfected with at least one gene which is expressed in the dendritic cells.

85. (Previously presented) The process of claim 84, wherein the gene is under the control of a promoter which initiates or upregulates gene expression on maturation of dendritic cells.

86. (Previously presented) The process of claim 84 or claim 85, wherein the gene is a reporter gene which expresses a detectable product in the dendritic cells.

87. (Previously presented) The process of claim 86, wherein the gene encodes a fluorescent product.

88. (Previously presented) The process of claim 87, wherein the gene is the GFP gene.

89. (Previously presented) The process of claim 71, wherein the ES cells are genetically modified so as to inactivate at least one copy of at least one gene.

90. (Previously presented) The process of claim 64, wherein the recovered immature dendritic cells are substantially pure.

91. (Previously presented) The process of claim 64, wherein the cells are lymphoid.

92. (Previously presented) The process of claim 64, wherein the cells are myeloid.

93. (Previously presented) The process of claim 64, wherein the cells are human.

94. (Previously presented) The process of claim 64, wherein the ES cells are derived from a mouse strain such as CBA/Ca or C57Bl/6.
95. (Previously presented) The process of claim 64, wherein the ES cells are from the ESF116 cell line.
96. (Withdrawn) A substantially pure population of immature dendritic cells obtainable by the process of claim 64.
97. (Withdrawn) A pharmaceutical composition comprising the population of claim 96 and a pharmaceutical excipient.
98. (Withdrawn) A method of treating a patient by immunotherapy which comprise administering to a patient an effective amount of the population of claim 96.
99. (Withdrawn) The method of claim 98, wherein the immunotherapy comprises immunotherapy.
100. (Withdrawn) The method of claim 99, wherein the immunostimulation comprises tumor immunotherapy or vaccination against infectious agents..
101. (Withdrawn) The method of claim 98, wherein the immunotherapy comprises down-modulation of a determinal immune response.
102. (Withdrawn) The method of claim 101, wherein the down-modulation of a determinal immune response is in the treatment of autoimmune disease or allograft rejection.
103. (Withdrawn) The method of claim 98, wherein the immunotherapy comprises altering dendritic cell function.

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104. (Withdrawn) The method of claim 98 or claim 103, wherein immunotherapy comprises inducing a Th1 to Th2 immune deviation.
105. (Previously presented) The process of claim 79, wherein the gene encodes FLIP or bcl-2.
106. (Previously presented) The process of claim 85, wherein the gene is a reporter gene which expresses detectable product in the dendritic cells.
107. (Previously presented) The process of claim 106, wherein the gene encodes a fluorescent product.
108. (Previously presented) The process of claim 107, wherein the gene is the GFP gene.
109. (Previously presented) The process of claim 103, wherein the immunotherapy comprises inducing a Th1 to Th2 immune deviation.
110. (New) The method of claim 64, wherein said composition further comprises GM-CSF.